Comparison of conventional magnetic resonance imaging and nonenhanced three dimensional time-of-flight magnetic resonance angiography findings between dogs with meningioma and dogs with intracranial histiocytic sarcoma: 19 cases (2010–2014)

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OBJECTIVE
To compare conventional MRI and nonenhanced 3-D time-of-flight (TOF) magnetic resonance angiography (MRA) findings between dogs with meningioma and dogs with intracranial histiocytic sarcoma (IHS).

DESIGN
Retrospective case series.

ANIMALS
14 dogs with meningioma and 5 dogs with IHS.

PROCEDURES
Medical records of dogs with meningioma or IHS that were examined at a tertiary veterinary hospital from 2010 through 2014 and underwent 3-D TOF MRA in conjunction with conventional MRI were reviewed. Findings for conventional MRI and 3-D TOF MRA were compared between the 2 groups of dogs to evaluate whether there were any characteristics that could be used to differentiate meningioma from IHS.

RESULTS
Tumor type was significantly associated with signal intensity on conventional T2-weighted and fluid-attenuated inversion recovery MRI images; most meningiomas were hyperintense, and most IHSs were isointense or hypointense on those images. Tumor type was not associated with signal uniformity, tumor location, tumor origin, or the presence of edema, midline shift, or brain herniation. On MRA, blood vessels adjacent to the tumor were identified and characterized for 9 of 14 dogs with meningioma and all 5 dogs with IHS. Vessels adjacent to meningiomas were displaced in 8 of 9 dogs, whereas vessels adjacent to IHSs were not displaced.

CONCLUSIONS AND CLINICAL RELEVANCE
Results indicated nonenhanced 3-D TOF MRA findings provided additional information that can be assessed in conjunction with conventional MRI findings to help differentiate meningiomas from IHSs in dogs. (J Am Vet Med Assoc 2016;248:1139–1147)
Small Animals

after initial examination,10 and 3 dogs that underwent surgery to remove the tumor died 2 days, 1 week, and 9 months after surgery.9 In a recent case series report,11 the survival times for 19 dogs with IHS ranged from 1 to 92 days (median, 3 days); this included dogs that were treated with surgery, radiotherapy, or chemotherapy.

Although meningioma and IHS have similar MRI characteristics, their response to treatment and prognosis differ greatly. It is important to differentiate meningioma from IHS before treatment so owners can be provided with the most precise information about treatment options and prognosis. Unfortunately, the SI on T2W and T1W images, enhancement after injection of contrast medium, and presence of the dural tail sign are the same for both meningiomas and IHSs1,6–14; therefore, it is difficult to differentiate the 2 types of tumors on the basis of conventional MRI findings alone.

In human patients, angiography can be used to differentiate meningiomas from other types of tumors because meningiomas have characteristic angiographic features such as the displacement of adjacent blood vessels and the presence of multiple radial vascular branches.15 Of the many angiography methods available, the most commonly used technique for both screening and evaluating cranial vessels is nonenhanced 3-D TOF MRA, which is a noninvasive method that uses an MRI scanner and does not require injection of contrast medium.16 With nonenhanced 3-D TOF MRA, blood vessels become visible because stationary protons in the adjacent tissue become saturated from repeated excitation pulses and produce a low SI, whereas protons from flowing blood in the blood vessels are not affected by the excitation pulses and therefore are not saturated and generate a high SI.16,17 Thus, on the resulting images, blood vessels with a high SI appear white against a black, low-SI background. In human patients, 3-D TOF MRA has been used to confirm arterial displacement associated with intracranial meningioma19 and is a useful aid for the diagnosis of that type of tumor.

In veterinary medicine, nonenhanced 3-D TOF MRA has been used to accurately image the intracranial vessels of healthy dogs.19 To our knowledge, the use of nonenhanced 3-D TOF MRA to image the intracranial vessels of dogs with intracranial tumors has not been described. If meningiomas in dogs have the same characteristic angiographic features as meningiomas in human patients, they should be able to be visualized by the use of nonenhanced 3-D TOF MRA. Furthermore, use of that technique may be able to differentiate meningiomas from IHSs because, although both are classified as extra-axial tumors, their histopathologic site of origin differs.20–25 Thus, the characteristics of the tumor-associated blood vessels may differ between the 2 types of tumors and be detectable and differentiated by nonenhanced 3-D TOF MRA. The purpose of the study reported here was to compare conventional MRI and nonenhanced 3-D TOF MRA findings between dogs with meningioma and dogs with IHS. We hypothesized that 3-D TOF MRA findings could be used to differentiate meningiomas from IHSs in dogs.

Materials and Methods

Case selection

The Nihon University Animal Medical Center medical record database was searched from 2010 through 2014 to identify records of dogs in which meningioma or IHS was diagnosed on the basis of histologic or necropsy findings. Only dogs that underwent conventional MRI in conjunction with nonenhanced 3-D TOF MRA were included in the study.

Medical records review

For each dog included in the study, data obtained from the medical record included breed, sex, body weight, age at tumor diagnosis, and histologic results. All conventional MRI and 3-D TOF MRA images were also retrieved and reviewed.

MRI and MRA

Each dog was anesthetized and positioned in sternal recumbency. Magnetic resonance imaging was performed with a 1.5-T MRI scanner1 and knee coil.b Sagittal and transverse T2W, T1W, FLAIR, and postcontrast T1W images of the head were obtained for all dogs; dor-

Figure 1—Maximum-intensity MRA images obtained in the dorsal (A) and sagittal (B) planes for a 6-year-old Beagle with idiopathic epilepsy that had clinically normal arteries within the brain provided as a reference for comparison with MRA images for dogs with meningiomas and IHSs. Notice the vessels of the external carotid artery system have been eliminated from both images so that the BA, CCA, ICA, IEA, MCA, RCA, and RCEA can be identified. The left CCA, ICA, MCA, and RCEA have been eliminated from the sagittal image so that they do not interfere with visualization of the corresponding arteries on the right side. Ca = Caudal. Cr = Cranial. Le = Left. R = Right.
sal images were obtained for a few dogs. Concurrently, nonenhanced 3-D TOF MRA was performed with the following settings, which were developed on the basis of variables used for human patients and adjusted for the size of the canine head: repetition time, 40 milliseconds; echo time, 6.8 milliseconds; field of view, 13.5 X 13.5 cm; matrix, 192 X 192; slice thickness, 0.8 mm; number of slices, 112; and number of slabs, 2.

**Table 1**—Summary of SI and SU findings for meningiomas (n = 14) and IHSs (5) on various MRI images for 19 dogs that were examined at a tertiary veterinary hospital from 2010 through 2014.

<table>
<thead>
<tr>
<th>MRI variable</th>
<th>MRI image</th>
<th>SI* or SU† classification</th>
<th>Dogs with meningioma</th>
<th>Dogs with IHS</th>
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<tr>
<td>SI</td>
<td>T2W</td>
<td>Hyperintense</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Isointense</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypointense</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>T1W</td>
<td>Hyperintense</td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Isointense</td>
<td></td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Hypointense</td>
<td></td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>FLAIR</td>
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</tr>
<tr>
<td></td>
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<td>5</td>
<td>1</td>
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<tr>
<td></td>
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<td>3</td>
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<tr>
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<td>2</td>
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<tr>
<td></td>
<td></td>
<td>Heterogeneous</td>
<td>7</td>
<td>3</td>
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<tr>
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<td>FLAIR</td>
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<tr>
<td></td>
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<td></td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Postcontrast T1W</td>
<td>Homogeneous</td>
<td></td>
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<td>3</td>
</tr>
<tr>
<td></td>
<td>Heterogeneous</td>
<td></td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

Values represent the No. of dogs within a group that had that particular finding.

*Signal intensity relative to clinically normal cortical gray matter. †The SU was classified as homogeneous when > 50% of the entire tumor area was homogeneous on T2W, T1W, postcontrast T1W, and FLAIR images and heterogeneous otherwise.

**Figure 2**—Representative T2W (A and E), T1W (B and F), postcontrast T1W (C and G), and FLAIR (D and H) MRI images obtained in the transverse plane for a 12-year-old Pembroke Welsh Corgi with a meningioma (A through D) and a 9-year-old Pembroke Welsh Corgi with an IHS (E through H). In the T2W images, the meningioma had a hyperintense (relative to clinically normal gray matter) SI and heterogeneous (< 50% of the entire tumor was homogeneous) SU, whereas the IHS had a hypointense SI and heterogeneous SU. In the T1W images, the meningioma had an isointense SI and heterogeneous SU, whereas the IHS had a hypointense SI and homogeneous SU. In the postcontrast T1W images, the meningioma had a homogeneous SU, whereas the IHS had a heterogeneous SU (SI was not assessed in those images). In the FLAIR images, the meningioma had a hyperintense SI and a homogeneous SU, whereas the IHS had a hypointense SI and a heterogeneous SU. See Figure 1 for remainder of key.
All MRI and MRA images were reviewed by 2 neurologists and 1 radiologist who were unaware of each patient’s profile and histologic diagnosis. Tumor location, SI, SU, and origin; extent of peritumoral edema; and presence of the dural tail sign, midline shift, and brain herniation were evaluated on MRI images. The SI and SU within the tumor were assessed on the transverse image that most clearly identified the tumor and was the same in each sequence. The SI of the largest area within the tumor was graded as hyperintense, isointense, or hypointense relative to clinically normal cortical gray matter on T2W, T1W, and FLAIR images. The SU of the tumor was classified as homogeneous when > 50% of the entire tumor area was homogeneous on T2W, T1W, postcontrast T1W, and FLAIR images and heterogeneous otherwise. Peritumoral edema was classified as present or absent on FLAIR images on the basis of the definition provided in another study. When present, the extent of peritumoral edema was classified as peritumoral when it extended ≤ 10 mm beyond the tumor margin or diffuse when it extended > 10 mm beyond the tumor margin.

Magnetic resonance angiography data were postprocessed on a workstation to create maximum-intensity images. The vessels of the external carotid artery system were eliminated from the images to facilitate evaluation of the vessels of the vertebral and ICA systems. The course, size, and bifurcations of the RCA, MCA, CCA, RCEA, and ICA were subjectively evaluated by comparing the vessels on the left side with their counterparts on the right side (Figure 1).

Statistical analysis

Tumor SI on T2W, T1W, and FLAIR images and the extent of peritumoral edema on FLAIR images were compared between dogs with meningioma and dogs with IHS by use of independent \( \chi^2 \) tests. The tumor SU in each sequence, tumor origin, presence of the dural tail sign on postcontrast T1W images, and presence of midline shift and brain herniation were compared between dogs with meningioma and dogs with IHS by use of Fisher exact tests. All analyses were performed with commercially available statistical software, and values of \( P < 0.05 \) were considered significant.

Results

Dogs

Review of the medical records database revealed that 24 dogs with meningioma and 6 dogs with IHS were examined at the hospital from 2010 through 2014. Of those 30 dogs, the diagnosis was confirmed on the basis of histologic examination for 29 and on the basis of necropsy results for 1. Ten dogs with meningioma and 1 dog with IHS were excluded from the study because nonenhanced 3-D TOF MRA was not performed in conjunction with conventional MRI. Thus, the study included 14 dogs with meningioma and 5 dogs with IHS.
The 14 dogs with meningioma included 1 sexually intact male, 7 neutered males, 3 sexually intact females, and 3 spayed females with a mean age at tumor diagnosis of 10.6 years (range, 9 to 14 years) and mean weight of 9.6 kg (21.1 lb; range, 2.6 to 30 kg [5.7 to 66.0 lb]). Breeds represented included Miniature Dachshund (n = 4), Shetland Sheepdog (2), and Golden Retriever, Pembroke Welsh Corgi, Beagle, Wire Fox Terrier, Toy Poodle, Yorkshire Terrier, Chihuahua, and mixed breed (1 each).

The 5 dogs with IHS included 2 sexually intact males, 1 neutered male, and 2 spayed females with a mean age at tumor diagnosis of 9.6 years (range, 9 to 10 years) and mean weight of 11.9 kg (26.2 lb; range, 4.3 to 16.5 kg [9.5 to 36.3 lb]). Breeds represented included Pembroke Welsh Corgi (n = 3), Beagle (1), and Maltese (1).

**MRI findings**

All of the tumors evaluated had an extra-axial origin. Of the 14 meningiomas, 4 were located in the left frontal lobe, 6 were located in the right frontal lobe, 1 was located in the left parietal lobe, 1 was located in the right parietal lobe, 1 was located in the ventral brainstem, and 1 extended from the right occipital lobe into the cerebellum. Of the 5 IHSs, 1 was located in the left frontal lobe, 2 were located in the right frontal lobe, and 2 were located in the right temporal lobe. Five of the 14 meningiomas and 2 of 5 IHSs had a dural tail sign present. Edema was associated with all 19 tumors. The edema was classified as peritumoral (extended ≤ 10 mm beyond the tumor margin) for 7 of 14 meningiomas and 1 of 5 IHSs and as diffuse (extended > 10 mm beyond the tumor margin) for the remaining 7 meningiomas and 4 IHSs. The tumor was associated with a midline shift for 8 dogs with meningioma and all 5...
dogs with IHS; midline shift was not evaluated for 1 dog with meningioma. Brain herniation was present in 3 dogs with meningioma and 1 dog with IHS. The brain had herniated through the foramen magnum in 2 dogs with meningioma; 1 of those dogs also had transtentorial herniation and syringomyelia in the cervical portion of the spinal cord. The remaining dog with meningioma and 1 dog with IHS had transtentorial brain herniation. Brain herniation was not assessed for 1 dog with meningioma. The SI and SU findings on various MRI images were summarized (Table 1). The majority (9/14) of meningiomas had a hyperintense SI on T2W and FLAIR images, whereas the majority (4/5) of IHSs had either an isointense or hypointense SI on those images (Figure 2). The SU (homogeneous or heterogeneous) varied within each tumor type on T2W, FLAIR, and post-contrast T1W images; however, most of the meningiomas and all of the IHSs had a homogeneous SU on T1W images.

Tumor type was significantly associated with SI on T2W \( (P = 0.030) \) and FLAIR \( (P = 0.007) \) images. Tumor type was not significantly associated with SI on T1W images, SU on any sequence, or any other tumor effects (tumor location, origin, dural tail sign, edema, midline shift, or brain herniation).

**MRA findings**

All targeted vessels (right and left CCA, ICA, MCA, RCA, and RCEA, and the unpaired BA and IEA) were identified on maximum-intensity MRA images for 18 of 19 dogs. For the remaining dog, which had a meningioma in the right parietal lobe, only the BA, both CCAs, both ICAs, left MCA, left RCA, and right RCEA were identified.

A targeted vessel was identified adjacent to the tumor for 9 of the 14 dogs with meningioma and all 5 dogs with IHS. The vessel adjacent to the tumor and its course or direction of displacement (if present) were dependent on the location of the tumor (Figure 3). For the 6 meningiomas that were located in the right frontal lobe, the target vessel adjacent to the tumor was the ICA for 1, the right MCA for 1, and unidentified for the remaining 4 (the tumor was located between the olfactory recess and caudal portion of the frontal lobe \( n = 3 \) or in the Falx cerebri \( n = 1 \) in those 4 dogs). For the 4 meningiomas that were located in the left frontal lobe, the target vessel adjacent to the tumor was the ICA for 2 and the left MCA for the other 2. The vessel adjacent to the tumor was the right CCA for the meningioma located in the right parietal lobe, right RCEA for the meningioma that extended from the occipital lobe into the cerebellum, and BA for the meningioma located in the ventral brainstem. A target vessel was not identified adjacent to the meningioma located in left parietal lobe. The vessel adjacent to the tumor was the right MCA for the 4 IHSs located in either the right frontal or parietal lobe and the IEA for the IHS located in the left frontal lobe.
The IEA was displaced caudally in 3 dogs with a meningioma located in the olfactory recess of a frontal lobe, although its size and number of bifurcations did not appear to be affected. The course and size of the IEA were not affected in the dog with an IHS located in the left frontal lobe. The MCA was displaced medially and passed through the tumor for 2 dogs with a meningioma located in the caudal portion of a frontal lobe and was displaced caudally for 1 dog with a meningioma located in the caudal portion of the left frontal lobe. The MCA was not displaced in any of the dogs with IHS (Figure 4). The size of the MCA and the number of bifurcations in that vessel were not affected in any of the dogs with meningioma. However, the right MCA was hypertrophied or dilated in the 2 dogs with an IHS located in the right frontal lobe but remained unaffected in the 2 dogs with an IHS located in the right temporal lobe. For the dog with a meningioma in the right parietal lobe, the right CCA ran tortuously toward the tumor and was hypertrophied or dilated and had multiple bifurcations. For the dog with meningioma that expanded from the occipital lobe into the cerebellum, the right RCEA was not displaced but was hypertrophied or dilated and had multiple bifurcations (Figure 5). For the dog with a meningioma in the brainstem, the BA was displaced dorsally, but its size and number of bifurcations were not affected.

Discussion

Results of the present study suggested that non-enhanced 3-D TOF MRA findings in conjunction with conventional MRI findings may be useful for differentiating meningiomas from IHSs in dogs. In the present study, tumor type was significantly associated with SI on T2W and FLAIR images. The majority (9/14) of meningiomas and only 1 of 5 IHSs were hyperintense on T2W and FLAIR images. Conversely, 2 and 3 IHSs were hypointense on T2W and FLAIR images, respectively, whereas none of the meningiomas were hypointense on T2W and FLAIR images. Those findings were similar to those of other studies in that the SI on T2W images was generally classified as hyperintense and the SI on FLAIR images was never classified as hypointense for meningiomas, whereas the SI for most IHSs was classified as hypointense, isointense, or mixed. The SI for a meningioma in a dog of one case report was described as hyperintense and that for the dog of another case report was characterized as mixed (hyperintense and hypointense) on FLAIR images. Although the findings of the present study suggested that the SI on T2W and FLAIR MRI images might aid in the differentiation between meningioma and IHS, the study population, especially the dogs with IHS, was limited, which might have resulted in a type II error. Therefore, we feel that it is more conservative (and perhaps better) to conclude that the tumor SI on T2W and FLAIR images was not significantly associated with tumor type. In the present study and other studies, the SI on T1W images was hypointense for many IHSs; however, that finding was not specific for IHSs, and some meningiomas were hypointense on T1W images. Investigators of 1 study reported that the risk of brain herniation for rapidly growing IHSs was greater than that for meningiomas. In the present study, brain herniation was not associated with tumor type. Walmsley et al concluded that brain herniation was more closely associated with tumor volume and location than with tumor type. On the basis of the results of the present study, we concluded that brain herniation could occur with both meningioma and IHS.

Although meningiomas and IHSs are both classified as extra-axial tumors, their site of origin differs, and that origin can affect blood vessels in the subarachnoid space, which might be evident on MRA. Meningiomas originate in the arachnoid covering of the brain, which can affect the trajectory of the vessels that course through the subarachnoid space, whereas IHSs originate in the leptomeninges and adjacent cerebral parenchyma and therefore are unlikely to affect the trajectory of blood vessels through the subarachnoid space. However, some meningiomas can infiltrate the pia mater and cerebral parenchyma, and some IHSs can infiltrate the dura mater; therefore, blood vessel abnormalities evident on MRA might not be specific for either type of tumor.

In the present study, the blood vessel adjacent to the tumor varied depending on the location of the tumor. A similar finding has been described for meningiomas in human patients. Collectively, these findings suggest that tumor-associated vessels can be predicted on the basis of tumor location. Prediction of vessels to be targeted during MRA can be used to limit the imaging area and shorten the image acquisition time, which will decrease the amount of time patients need to be anesthetized.

Of the 14 dogs with meningioma in the present study, the blood vessel adjacent to the tumor could not be identified for 5. This was likely the result of the limited ability of nonenhanced 3-D TOF MRA images obtained with a 1.5-T scanner to identify vessels and attributed to the fact that the tumors in those dogs were located far from vessels that could be identified by the MRA protocol used. For the remaining 9 dogs with meningioma, blood vessels identified adjacent to the respective tumors included the BA, CCA, IEA, MCA, and RCEA. In 8 of those 9 dogs, the blood vessel adjacent to the tumor was displaced. The displacement of those vessels was attributed to a mass effect and arterial involvement with the tumor. The tortuous nature of the CCA that was adjacent to the meningioma in 1 dog was comparable to that observed for vessels that supply meningiomas in human patients.

The blood vessel adjacent to the tumor was identified for all 5 dogs with IHS in the present study, and those vessels identified included the IEA and MCA.
Unlike the dogs with meningioma, none of the vessels adjacent to an IHS were displaced.

In human patients with meningioma, blood vessels that supply the tumor are generally hypertrophied and tortuous and have several bifurcations. In the present study, the vessel adjacent to the tumor was described as hypertrophied or dilated for only 2 dogs with meningioma and 2 dogs with IHS. The hypertrophied or dilated vessels associated with the meningiomas also had multiple bifurcations, whereas those associated with the IHSs did not. The nonenhanced 3-D TOF MRA method used in the present study cannot identify the vascular supply of a tumor. If it is assumed that the morphology of the blood vessels that supply extra-axial intracranial tumors in dogs is similar to that for meningiomas in human patients, then the vessels that were characterized as hypertrophied or dilated in the present study may have represented the primary vessels that supplied the respective tumors. The fact that the hypertrophied or dilated vessels associated with IHSs approached the tumor in a linear fashion without any bifurcations, whereas the hypertrophied or dilated vessels associated with meningiomas had multiple bifurcations, might represent a characteristic difference that can be used to differentiate the 2 tumor types.

In the present study, nonenhanced 3-D TOF MRA findings provided additional information that can be assessed in conjunction with conventional MRI findings to help differentiate meningiomas from IHSs in dogs. Identification of blood vessels by use of nonenhanced 3-D TOF MRA is limited, and that methodology cannot be used to visualize and define the vascular supply of an intracranial tumor. Contrast MRA, CT angiography, and selective angiography with a vascular catheter are necessary for accurate and precise evaluation of intracranial vessels. Unfortunately, those methods are more invasive than nonenhanced 3-D TOF MRA. Therefore, further studies that involve larger study populations than that of the present study are necessary to better elucidate the use of nonenhanced 3-D TOF MRA for differentiation of meningioma from IHS in dogs.

Footnotes

a. EXCELART Vantage; Toshiba, Tokyo, Japan.
b. QD knee coil, Toshiba, Tokyo, Japan.
c. Virtual Place, AZE, Tokyo, Japan.
d. GraphPad Prism 5, GraphPad Software Inc, La Jolla, Calif.

References


From this month’s AJVR

Ultrasonographic predictors of response of European eels (Anguilla anguilla) to hormonal treatment for induction of ovarian development
Anna V. Müller et al

OBJECTIVE
To examine ultrasonographic predictors of ovarian development in European eels (Anguilla anguilla) undergoing hormonal treatment for assisted reproduction.

ANIMALS
83 female European eels.

PROCEDURES
Eels received weekly IM injections of salmon pituitary extract (first injection = week 1). Ultrasonography of the ovaries was performed twice during hormonal treatment (weeks 7 and 11). Eels were identified on the basis of body weight as having an adequate response by weeks 14 to 20 or an inadequate response after injections for 21 weeks. Eels were euthanized at the end of the experiment and classified by use of ovarian histologic examination. Ovarian cross-sectional area and size of eel (ie, length?) were used to classify eels (fast responder, slow responder, or nonresponder) and to calculate an ultrasonographic-derived gonadosomatic index. Gray-level co-occurrence matrices were calculated from ovarian images, and 22 texture features were calculated from these matrices.

RESULTS
The ultrasonographic-derived gonadosomatic index differed significantly between fast responders and slow responders or nonresponders at both weeks 7 and 11. Principal component analysis revealed a pattern of separation between the groups, and partial least squares discriminant analysis revealed signals in the ovarian texture that discriminated females that responded to treatment from those that did not.

CONCLUSIONS AND CLINICAL RELEVANCE
Ovarian texture information in addition to morphometric variables can enhance ultrasonographic applications for assisted reproduction of eels and potentially other fish species. This was a novel, nonlethal method for classifying reproductive response of eels and the first objective texture analysis performed on ultrasonographic images of the gonads of fish. (Am J Vet Res 2016;77:478–486)